The first of the second of the

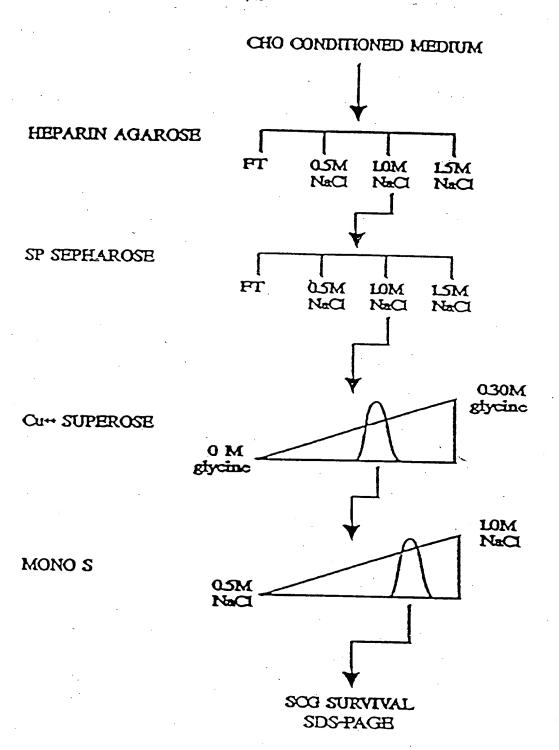
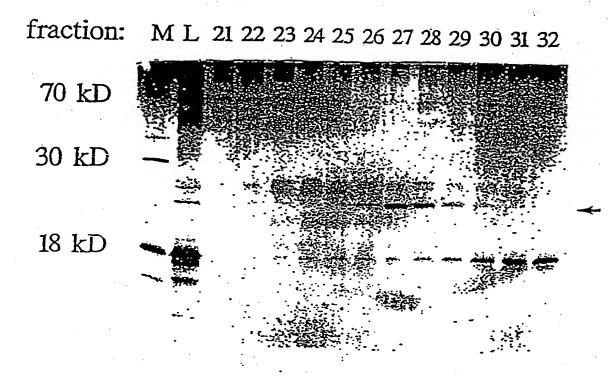


Figure 1



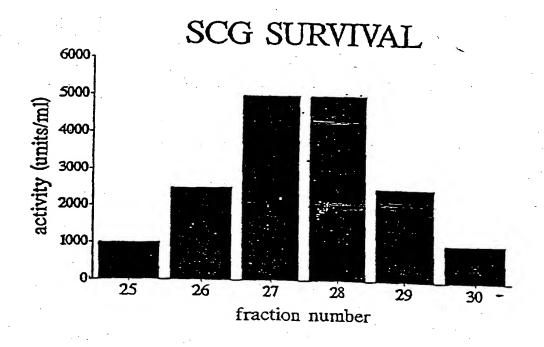


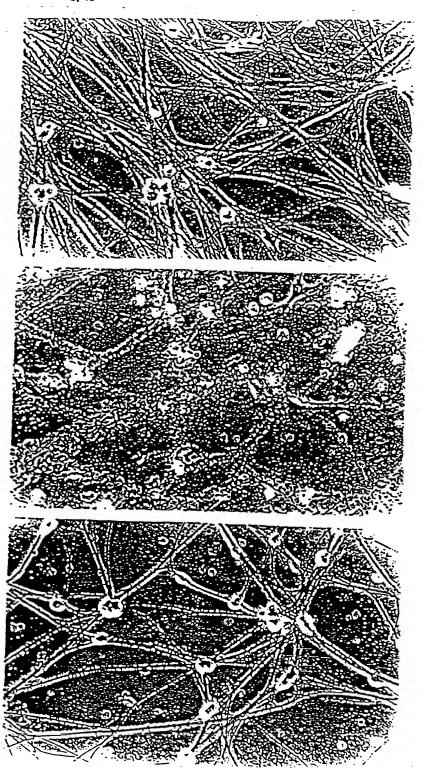
Figure 2

A) NGF

B) Anti-NGF

C) Anti-NGF

The Neurturin



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Figure 4

The state of the s

```
S P D K Q H A V L P R R E R N R Q A A A N P E N S R G K G HGDNF
                    DKQAAALPRRERNRQAAAASPENS
            SP
                                                                                                                         R G K G MGDNF
                    DKQAAALPRRERNRQAAAASPENSRGKG
                                                                                                                                           rGDNF
  1
                                                                                                                                           HNTN
                                                                                                                                           MINM
          RRGQRGKNRGC
RRGQRGKNRGC
RRGQRGKNRGC
---ARLGARPC
---PGARIPC
                                                       V L T A I H L N V T O L G L G Y E T K V L T A I H L N V T O L G L G Y E T K V L T A I H L N V T D L G L G Y E T K G L R E L E V R V S E L G L G Y A S D G L R E L E V R V S E L G L G Y T S O
 31
                                                                                                                                 TK HGONF
 31
                                                                                                                                          mGDNF
                                                                                                                                          rGDNF
 1
                 LIFRYCSGSCDAAETTYDKILKNLSRNR hGDNALIFRYCSGSCESAETMYDKILKNLSRSR MGDNALIFRYCSGSCEAAETMYDKILKNLSRSR MGDNALIFRYCAGACEAAARVYDLGLRRLRQRR HNTNVLFRYCAGACEAAIRIYDLGLRRLRQRR MNTN
 61
                                                                                                                                          hGDNF
 61
 61
                                                                                                                                          mGDNF
                                                                                                                                          rGDNF
28
26
        R L V S D K V - G Q A C C R P I A F R L T S D K V - G Q A C C R P V A F R L T S D K V - G Q A C C R P V A F R L R R E R V R A Q P C C R P T A Y R V R R E R A R A H P C C R P T A Y
                                                                                    D D D L S F L D D N L V D D D L S F L D D N L V D D D L S F L D D S L V E D E V S F L D A H S R E D E V S F L D V H S R
                                                                                                                   D D N L V
                                                                                                                                         hGDNF
91
91
                                                                                                                                         mGDNF
                                                                                                                                         rGDNF
58
                                                                                                                                         HNTH
       Y H I L R K H S A K R C G C I .
Y H I L R K H S A K R C G C I .
Y H I L R K H S A K R C G C I .
Y H T V H E L S A R E C A C V .
Y H T L Q E L S A R E C A C V .
120
                                                                                                                                         hGDNF
                                                                                                                                         mGDNF
120
88
                                                                                                                                         rGDNF
                                                                                                                                         HNTN
                                                                                                                                         NTNm
```

Figure 5

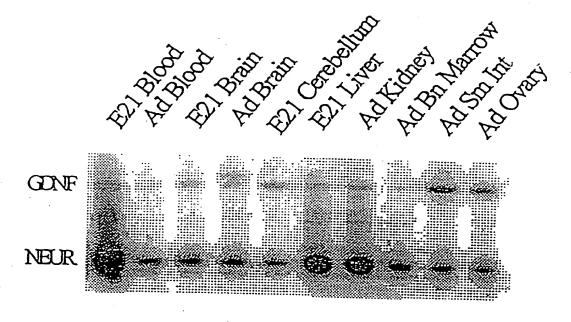


Figure 6

Met Gin Arg Trp Lys Ala Ala Ala Leu Ala Ser Val Leu Cys Ser Ser Val Leu Ser Ile	60
TGGATGTGTCGAGAGGGCCTGCTTCTCAGCCACCGCCTCGGACCTGCGCTGGTCCCCCTG Trp Met Cys Arg Glu Gly Leu Leu Leu Ser His Arg Leu Gly Pro Ala Leu Val Pro Leu	. 10/
CACCGCCTGCCTCGAACCCTGGACGCCCGGATTGCCCGCCTGGCCCAGTACCGTGCACTC His Arg Leu Pro Arg Thr Leu Asp Ala Arg Ile Ala Arg Leu Ala Gin Tyr Arg Ala Leu	
CTGCAGGGGCCCCGGATGCGATGGAGCTGCGCGAGCTGACGCCCTGGGCTGGGCGCCC Leu Gin Giy Ala Pro Asp Ala Met Giu Leu Arg Giu Leu Thr Pro Trp Ala Giy Arg Pro	240
CCAGGTCCGCCGTCGGGGGGGCCCCCGGCGCGCGCGCGCG	300
Pro Gly Pro Arg Arg Ala Gly Pro Arg Arg Arg Ala Arg Ala Arg Leu Gly Ala	000
CGGCCTTGCGGGCTGCGCGAGCTGGAGCTGAGCGAGCTGGGCCTACGCG	360
Arg Pro Cys Gly Leu Arg Glu Leu Glu Val Arg Val Ser Glu Leu Gly Leu Gly Tyr Ala	200
TCCGACGAGACGGTGCTGTTCCGCTACTGCGCAGGCGCCTGCGAGGCTGCCGCGCGCG	" 20
Ser Asp Glu Thr Val Leu Phe Arg Tyr Cys Ala Gly Ala Cys Glu Ala Ala Ala Arg Val	420
TACGACCTCGGGCTGCGACGACTGCGCCAGCGGCGGCGCGCGGGGGGGG	1180
Tyr Asp Leu Gly Leu Arg Arg Leu Arg Gln Arg Arg Arg Leu Arg Arg Glu Arg Val Arg	400
GCGCAGCCCTGCTGCCGCCCGACGGCCTACGAGGACGAGGTGTCCTTCCT	EIIO
Ala Gin Pro Cys Cys Ang Pro Thr Ala Tyr Giu Asp Giu Val Ser Phe Leu Asp Ala His	OPG
AGCCGCTACCACACGGTGCACGAGCTGTCGGCGCGCGAGTGCGCCTGCGTGTGA 594	
Ser Arg Tyr His Thr Val His Glu Leu Ser Ala Arg Glu Cys Ala Cys Val	

Figure 7

Met Arg Arg Trp Lys Ala Ala Leu Val Ser Leu Ile Cys Ser Ser Leu Leu Ser Val	60
TGGATGTGCCAGGAGGGTCTGCTCTTGGGCCACCGCCTGGGACCCGCGCTTGCCCCGCTA Trp Met Cys Gln Glu Gly Leu Leu Leu Gly His Arg Leu Gly Pro Ala Leu Ala Pro Leu	120
CGACGCCCTCCACGCACCCTGGACGCCCGCATCGCCCGCC	: 180
CTCCAGGGCGCCCCGACGCGGTGGAGCTTCGAGAACTTTCTCCCTGGGCTGCCCGCATC Leu Gin Gly Ala Pro Asp Ala Val Giu Leu Arg Giu Leu Ser Pro Trp Ala Ala Arg Ile	240
CCGGGACCGCGCGTCGAGCGGGTCCCCGGCGTCGGCGGGGGCTCGGCCT	300
Pro Gly Pro Ang Ang Ang Ala Gly Pro Ang Ang Ang Ang Ala Ang Pro Gly Ala Ang Pro	300
TGTGGGCTGCGCGAGCTCGAGGTGCGCGTGAGCGAGCTGGGCCTGGGCTACACGTCGGAT	000
Cys Gly Leu Arg Glu Leu Glu Val Arg Val Ser Glu Leu Gly Leu Gly Tyr Thr Ser Asp	360
GAGACCGTGCTGTTCCGCTACTGCGCAGGCGCGTGCGAGGCGGCCATCCGCATCTACGAC	
Glu Thr Val Leu Phe Arg Tyr Cys Ala Gly Ala Cys Glu Ala Ala Ile Arg Ile Tyr Asp	420
CTGGGCCTTCGGCGCCTGCGCCAGCGGAGGCGCGCGCGCG	" 00
Leu Gly Leu Arg Arg Leu Arg Gln Arg Arg Arg Val Arg Arg Glu Arg Ala Arg Ala His	400
CCGTGTTGTCGCCCGACGGCCTATGAGGACGAGGTGTCCTTCCT	EUO
Pro Cys Cys Arg Pro Thr Ala Tyr Glu Asp Glu Val Ser Phe Leu Asp Val His Ser Arg	040
ACCACACGCTGCAAGAGCTGTCGGCGCGGGAGTGCGCGTGCGT	
Tyr His Thr Leu Gln Glu Leu Ser Ala Arg Glu Cys Ala Cys Val •	

GGAGGGAGAGCGCGGGGGGTTTCGTCCGTGTGCCCCGCGCGCG	-301
TCCTCGCGTGCCCCGCGTCCTGAGCGCGCTCCAGCCTCCCACGCGCGCC	-251
ACCCCGGGGTTCACTGAGCCCGGCGAGCCCGGGGAAGACAGAGAAAGAGA	-201
GGCCAGGGGGGAACCCCATGGCCCGGCCCGTGTCCCGCACCCTGTGCGG	-151
TGGCCTCCTCCGGCACGGGTCCCCGGGTCCCCGCGATCC	-101
GGATGGCGCACGCAGTGGCTGGGGCCGGGCCCGGGCTCGGGTCGGAGG	-51
AGTCACCACTGACCGGGTCATCTGGAGCCCGTGGCAGGCCGAGGCCCAGG	-1
ATGAGGCGCTGGAAGGCAGCGCCCTGGTGTCGCTCATCTGCAGCTCCCT	50
GCTATCTCTGGATGTGCCAGGAGGGTCTGCTCTTGGGCCACCGCCTGG	100
GACCCGCGCTTGCCCCGCTACGACGCCCTCCACGCACCCTGGACGCCCGC	150
ATCGCCCGCCTGGCCCAGTATCGCGCTCTGCTCCAGGGCGCCCCCGACGC	200
GGTGGAGCTTCGAGAACTTTCTCCCTGGGCTGCCCGCATCCCGGGACCGC	250
GCCGTCGAGCGGGTCCCCGGCGTCGGCGGGGCCCGGGGGCTCGGCCT	300
TGTGGGCTGCGCGAGCTCGAGCTGAGCGAGCTGGGCCTA	350
CACGTCGGATGAGACCGTGCTGTTCCGCTACTGCGCAGGCGCGTGCGAGG	400
CGGCCATCCGCATCTACGACCTGGGCCTTCGGCGCCTGCGCCAGCGGAGG	4 50
CGCGTGCGCAGAGAGCGGGCGCGCGCGCCGCCGTGTTGTCGCCCGACGGC	500
CTATGAGGACGAGGTGTCCTTCCTGGACGTGCACAGCCGCTACCACACGC	550
TGCAAGAGCTGTCGCCGCGGGAGTGCGCGTGCGTGATGCTACCTCACG	600
CCCCCGACCTGCGAAAGGGCCCTCCCTGCCGACCCTCGCTGAGAACTGA	650
CTTCACATAAAGTGTGGGAACTCCC	675

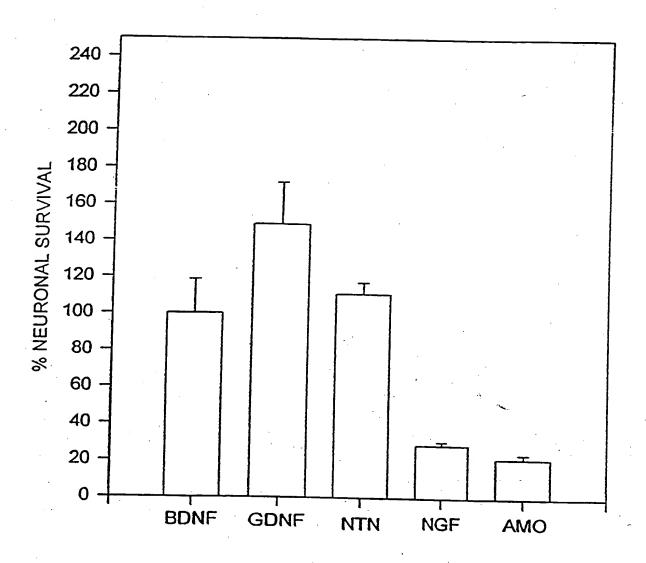


Figure 10

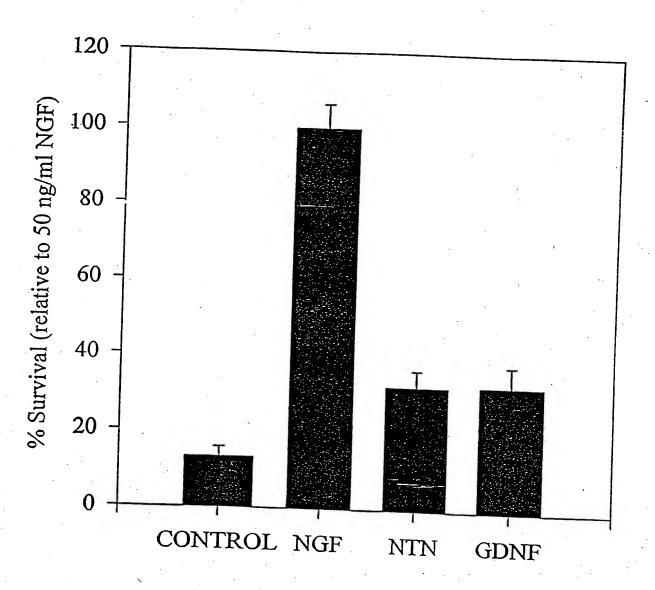


FIGURE 11



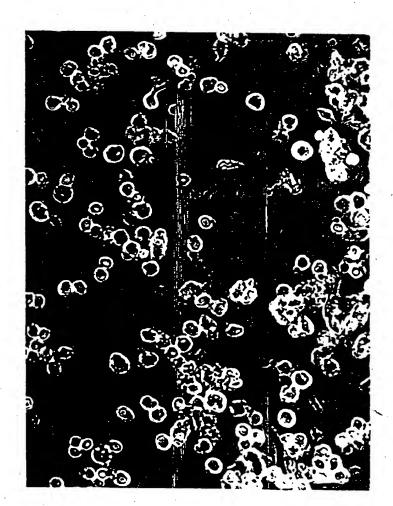


FIGURE 13 A. Untreated



FIGURE 13 B. Neurturin-treated

MAPK Response in Neuroblastoma Cell Lines

SK-NSH Neuroblastoma (naive)

FIGURE 14A

'IGURE 14B NGP Neuroblastoma (RA tx)



'IGURE 14C

SY5Y Neuroblastoma (RX tx)

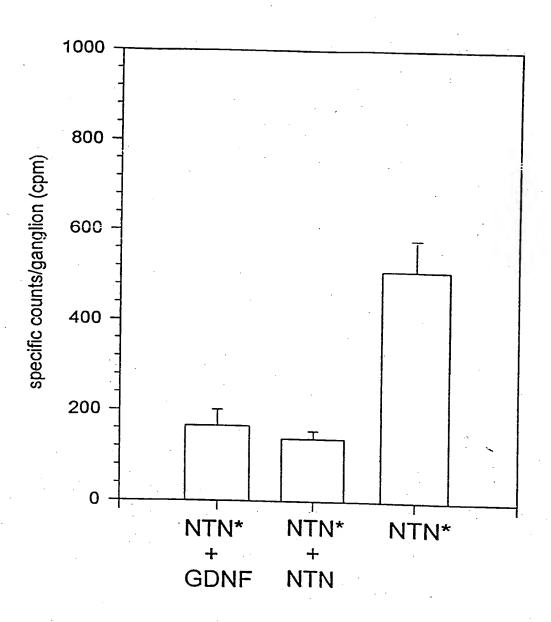


FIGURE 15

FIGURE 16

	,
	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
H R SEQUENCE	CCVRQLYIDFRKDLGWK-WIHEPKGYHANFCLGPCEYIWSLDTQYSKVLALYNQHNPGASAA-P CCLRPLYIDFRKDLGWK-WIHEPKGYYANFCAGACPYLWSSDTQHSRVLSLYNTINPEASAS-P CCVRPLYIDFRADLGWK-WIHEPKGYYANFCAGACPYLMSSDTQHSRVLSLYNTINPEASAS-P CCVRPLYIDFRADLGWK-WHEPKGYYANFCAGPCPYLRSADTTHSTVLGLYNTLNPEASAS-P CCKRQFFVSFK-DIGWNDWIIAPEGYYGNYCEGECPHIAA:-VPGSASSFHTAVVNQYRWRGLNP-GTVNS CCRQFFIDFR-LIGWNDWIIAPEGYYGNYCEGECPHYAA:-VPGSASSFHTAVNQYRWRGLNP-FTANIK CCRQFFIDFR-LIGWNDWIIAPEGYYGNYCEGECPHYAG:-VPGSASSFHTAVNQYRWRGLNP-VPST CCRRHELYVDFS-DVGWNDWIVAPPGYQAFYCHGECPPLADHLNSTNHAIVQTLVNSVNS-Y-IPKA CRRHELYVSFR-DLGWQDWIIAPEGYAAFYCDGECSFPLADHKNSTNHAIVQTLVNSVNS-S-IPKA CRRHELYVSFR-DLGWQDWIIAPEGYAAFYCDGECSFPLADHKNSTNHAIVQTLVNISVNS-V-PKP CKKHELYVSFR-DLGWQDWIIAPEGYSAAYYCEGECSFPLADHKNATNHAIVQTLVHLMNPBT-VPKP CKKHELYVSFR-DLGWQDWIIAPEGYSAAYYCEGECSFPLNAHMNATNHAIVQTLVHLMNPBT-VPKP CKKHELYVSFR-DLGWQDWIIAPEGYSAYYCEGECSFPLNAHMNATNHAIVQTLVHLMPPBT-VPKP CKRHELYVSFR-DLGWQDWIIAPEGYSAYYCEGECSFPLNAHMNATNHAIVQTLVHLLEPKK-VPKP CKRRHILYVSFR-DLGWQDWIIAPEGYSAYYCEGECSFPLNAHMNATNHAIVQTLVHLLEPKK-VPKP CRRREILYVSFR-DLGWGDWIIAPEGYSAYYCEGECSFPLNAHMNATNHAIVQTLVHLLANPTA-VPKP CKRRHILYVSFR-DLGWGDWIIAPEGYSAYYCEGECSFPLNAHMNATNHAIVQTLVHLANPTA-VPKP CRRREILYVSFR-DLGWGDWIIAPEGYSAYYCEGECSFPLNAHMNATNHAIVQTLVHLANPTA-VPKP CRRRILIYVSFR-DLGWGNWIIAPRGFWANYCHGECSFPLNAHALSGSGPPALNHAAVLRAAAPGA-ADLE CRRRILIYVSFR-BUGWNHWIAPRGFWANYCHGECEPFPLTDNVTFTKHAIVQTLVHGNPK-ASKA CRRTSLHVNFK-BIGMDSWIIAPEGYGGCLHPPRINAHMNATNHAILQSIVAHAMADA-ABCA CRRTSLHVNFK-BIGMDSWIIAPEGYGGCCHPRQCIHIPPNLSLEVPRAPAPPTAAQPYVELLENRPGPORAPPA-ASKA CRRTSLHVNFK-BIGMDSWIIAPEGYGGCCHPRQCIHIPPNLSLEVPRAPAPPTAARONNYE
GROWTH	TGF81 TGF83 TGF83 INHBA INHBB NODAL BMP2 BMP4 DPP BMP6 BMP7 BMP6 BMP7 BMP7 BMP7 BMP8 GOA BMP3 VG1 CDF1 GDF1 GDF3 NG1 NHC NINHC NTN
SEQ ID NO:	8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8

FIGURE 1

CDOME	
FACTOR	SEQUENCE
mana.	
	CCVPQALEPLPIVYYVGRKPKVEQLSNMIVRSCKCS
TGF\$2	CCVSQDLEPLTILYYIGKTPKIEQLSNMIVKSCKCS
TGF63	CCV - PODIEDITII VIII CREPTE - EQUISNMI VKSCKCS
	CCVPQDLEPLTILYYVGRTPKVEQLSNMVVKSCKCS
	CCA - EIVTKEWSMTAADDGUNTI-KKDIOMMIMEEGGGG
	CCT - FINDSIMOMLY FIDDRYNTWITTER COCK
NODAL	CCAPVKTKPLSMLYVDNGRVLLEHHKDMIVEECGCL
BMP2	CCV PTELSAIGMIVI DENDICATE VILLEHAKDMIVEECGCL
RMD4	CCVPTELSAISMLYLDENEKVVLK-NYQDMVVEGCGCR
-	
	CCV - PIQLUSVAMLYLNDOSTRATIK-NVOEMURAGGGG
	CCA - FIRMAISVLYFDDSSNVTIK-KVDMMAADOGGG
BMP6	CCAPTKLNAISVLYFDDNSNVILK-KYRNMVVRACGCH
BMP7	CCAPTQLNAISVLYFDDSSNVILK-KYRNMVVRACGCH
BMP8	CCA - PTVI CATCUT VVD CCATTON
	CCAPTKLSATSVLYYDSSNNVILR-KHRNMVVKACGCH
	CCAPTRLGALPVLYHLNDENVNLK-KYRNMIVKSCGCH
	CCV PEKMSSLSILFFDENKNNNT RN - VDNMMVID GD GD
	CCVPIAMSPISMLEYDNNDNTAT.D-UVENMATEDEGGE
	CCVPARLSPISVLFFDNSDNVVLR-QYEDMVVDECGCR
GDF3	VCVPTKLSPISMLYQDSDKNVILR-HYEDMVVDECGCG
DORSLN	CCVPTKLDAIGII VVDDAGUDET
TNHO	CCVPTKLDAISILYKDDAGVPTLIYNYEGMKVAECGCR
	CCAALPGTMRPLHVRTTSDGGYSFKYETVPNLLTQHCACI
	CCVPIAIIGKLLISLSEERTSAHHUDNMUATECCCD
	SCVPGKYSPLSVLTIEPDGSTAVK-FVFDMMATGGTGD
GDNF	CCRPIAFD-DDLSFLDDNLVYHILRKHSAKRCGCI
NTN	CCRPTAVE DEVICEI DANS PRINCEINE DE L'ANNE DE L
	CCRPTAYE-DEVSFLDAHSRYHTVHELSARECACV
	BMP4 DPP BMP5 BMP6 BMP7 BMP8 60A BMP3 VG1 GDF1 GDF3 DORSLN INH MIS GDF9 GDNF

FIGURE 18